Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Claims 119-138 are pending in this application and are rejected/objected to on various grounds. Claims 127-128, 132-134 have been canceled without prejudice or disclaimer to claim their subject matter in subsequent continuation or divisional applications. Claims 139-142 have been added, support for which is found in canceled Claim 132 and in the instant specification at page 285, line 11 onwards. Entry of these claims is respectfully requested. Accordingly, Claims 119-126, 129-131, 135-142 are now pending in this application. Claims 119-128 have been amended for clarity with the recitation "wherein said nucleic acid is amplified in lung or colon cancers," support for which is found in Example 170 of the instant specification, especially on Table 8 and 9B. The rejections to the presently pending claims are respectfully traversed.

Specification

The disclosure was objected to by the Examiner as containing "embedded hyperlink and/or other form of browser-executable code." The foregoing amendment to the specification which deleted all embedded hyperlinks, is believed to overcome the present objections.

In addition, amendments to the specification have incorporated the requisite assurances that "all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the pertinent U.S. patent."

Accordingly, Applicants believe that all objections to the specification has been overcome.

Continuity

The Examiner asserts that Applicants have not complied with conditions to receive benefit of an earlier filing date under 35 U.S.C. 119(e) because allegedly, the provisional applications listed in the first paragraph of the instant application do not refer to SEQ ID NO: 348 or 349, PRO1097. Applicants respectfully traverse.

Applicants submit that they rely on the gene amplification assay for patentable utility of the PRO1097 molecule, its antibodies and nucleic acids encoding it, which was first disclosed in U.S. Provisional Application 60/141037, filed June 23, 1999, priority to which has been claimed

in this application. Applicants note that the sequences disclosed in the U.S. Provisional Application No. 60/141,037 have a different sequence listing and a different Figure numbering from that of the current application; therefore, the sequence of PRO1097 is listed as SEQ ID NO: 41 and 42, and Figure 29 and 30 in U.S. Provisional Application 60/141,037. Hence, Applicants are entitled to the benefit of the above provisional application and accordingly, to an effective filing date of at least **June 23, 1999.** The Examiner is respectfully requested to reconsider this application's priority based on this clarification.

Claim Rejections – 35 U.S.C. §101 and §112, First Paragraph

Claims 119-138 were rejected under 35 U.S.C. §101 since allegedly "because the claimed invention lacks a credible, specific and substantial asserted utility or a well-established utility." Claims 119-138 were further rejected under 35 U.S.C. §112, first paragraph, allegedly "since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention".

Regarding the gene amplification data, the Examiner acknowledges that there is amplification of DNA59841-1460 in several epithelial tumors on page 7 of the Office Action but asserts that "a slight increase in clone copies in several tumor types is not indicative of a specific or substantial utility for PRO1097 for use as an agent to detect or treat cancer." The Examiner quotes articles like Hittelman *et al.* and Crowell *et al.* to show that an increase in chromosome number is a common characteristic of cancerous and non-cancerous epithelial cells and therefore utility may not be claimed and the Examiner concludes that the asserted utility is not substantial. The Examiner further quotes Pennica *et al.*, and Haynes *et al.* to show that "it does not necessarily follow that an increase in gene copy number results in increased gene expression and increase protein expression, such that the antibodies would be useful diagnostically or as a target for cancer drug development". For the reasons outlined below, Applicants respectfully disagree.

Initially, Applicants submit that they rely on the gene amplification assay for patentable utility of the nucleic acids encoding PRO1097 molecule in the instant application, which was first disclosed in U.S. Provisional Application No. 60/141037, filed June 23, 1999, priority to which has been claimed in this application. Applicants further submit that the cancellation of

Claims 127-128 and 132-134, without prejudice or disclaimer, renders this rejection moot to these claims. Further, without acquiescing to the propriety of this rejection, Applicants have amended Claims 119-123 to recite a functional recitation: "wherein said nucleic acid is amplified in lung or colon cancer."

Applicants submit that Hittelman *et al.* and Crowell *et al.* in fact show that an increase in chromosome number is a common characteristic of cancerous and **pre**-cancerous epithelial cells and therefore, increase in chromosome number or gene amplification is useful as a marker for a cancerous or pre-cancerous state. This is a substantial and credible utility. Further, since the data obtained for PRO1097 pertains to lung or colon cancers, as is instantly claimed, the utility is specific as well.

Further, in response to the Examiner's rejections based on Pennica and Haynes, Applicants entirely disagree with the Examiner's conclusion that "although the specification teaches that PRO1097 is expressed in several epithelial cancers (Table 9B), the state of the art is such that **protein** expression levels cannot be accurately predicted from the level of corresponding mRNA transcript, and therefore cannot be correlated to antibody binding" (emphasis added). More importantly, Applicants respectfully point out that the instantly amended claims are directed to naturally occurring **nucleic acids** encoding PRO1097 that are amplified in lung or colon cancer, and not to polypeptides or mRNA - products of gene expression. Hence, in this instance, this rejection which addresses gene/ polypeptide expression based on the teachings of Pennica *et al.*, and Haynes *et al.*, is improper. For the sake of brevity, since "gene expression or polypeptide expression" have no bearing on the instant claims, Applicants do not discuss the reasons why they disagree with the Examiner's conclusions further.

Instead, Applicants submit that, based on the instant disclosure, which details how to make and use nucleic acid variants (see pages 308-311), and the advanced knowledge in the art at the time of filing, one skilled in the art would know exactly what nucleic acid variants the instant claims encompass and would know how to make and use these nucleic acids for the diagnosis of lung or colon cancers without undue experimentation; for example, by using diagnostic methods based on hybridization to such amplified sequences.

Applicants have demonstrated utility for the PRO1097 nucleic acid as a lung or colon cancer tumor marker. Accordingly, the present 35 U.S.C. §101and §112, first paragraph, utility rejections should be withdrawn.

Claim Rejections - 35 U.S.C. § 112, First Paragraph - Written Description

Claims 119-124 and 132-138 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of filing, had possession of the claimed invention. Applicants respectfully traverse this rejection to the pending claims.

The Legal Standard for Written Description

The well- established test for sufficiency of support under the written description requirement of 35 U.S.C. §112, first paragraph, is whether the disclosure "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *In re* Kaslow, 707 F.2d 1366, 1375, 212 USPQ 1089, 1096 (Fed. Cir. 1983); see also Vas-Cath, Inc. v. Mahurkar, 935 F. 2d at 1563, 19 USPQ2d at 1116 (Fed. cir. 1991). The adequacy of written description support is a factual issue and is to be determined on a case-by-case basis. see *e.g.,* Vas-Cath, Inc. v. Mahurkar, 935 F. 2d at 1563, 19 USPQ2d at 1116 (Fed. cir. 1991). The factual determination in a written description analysis depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure. Union Oil v. Atlantic Richfield Co., 208 F. 3d 989, 996 (Fed. Cir. 2000).

Arguments

As noted above, whether the Applicants were in possession of the invention as of the effective filing date of an application is a factual determination, reached by the consideration of a number of factors, including the level of knowledge and skill in the art, and the teaching provided by the specification. The inventor is not required to describe every single detail of his/her invention. An Applicant's disclosure obligation varies according to the art to which the invention pertains.

The present invention pertains to the field of recombinant DNA/protein technology. It is well established that the level of skill in this field is very high since a representative person of skill is generally a Ph.D. scientist with several years of experience. Accordingly, the teaching imparted in the specification must be evaluated through the eyes of a highly skilled artisan as of the date the invention was made. The instant invention, defined by the claims, concerns nucleic acids having 80%, 85%, 90%, 95% or 99% sequence identity with the disclosed nucleic acid sequence SEQ ID NO: 348 and further recite the functional recitation: "wherein said nucleic acid is amplified in lung or colon cancer." Based on the detailed description of the cloning and expression of variants of PRO1097 in the specification, the description of the gene amplification assay and description of the testing of variant nucleic acids in the assay, the actual reduction to practice of sequence SEQ ID NO: 348 and the functional recitation in the instant claims, Applicants submit that one of skilled in the art would know that Applicants possessed the invention as claimed in the instant claims.

Hence, Applicants submit that this rejection should be withdrawn.

Claim Rejections - 35 U.S.C. §112, First Paragraph - Deposit Rules

Claims 119-138 are rejected under 35 U.S.C. §112, first paragraph, as not complying with the enablement requirement. The Examiner asserts that the deposit made under DNA59841-1460 must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public.

Applicants submit that a deposit was made at ATCC under the ATCC accession number 203044 for this DNA. Further, amendments to the specification have (1) the current ATCC address; and (2) incorporated the requisite assurances that "all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the pertinent U.S. patent." Thus, the material is available by a repeatable method, as set forth in the specification and thus, Applicants comply with the enablement requirement and this rejection should be withdrawn.

Claim Rejections – 35 U.S.C. §112, Second Paragraph

Claims 119-138 were rejected under 35 U.S.C. §112, second paragraph, for being indefinite. The Examiner asserts that these claims are rendered indefinite because of the phrase "extracellular domain" and further, claims 132 and 133 are rendered indefinite because of the phrase "stringent conditions."

Applicants submit that references to the term "extracellular domain" have been removed in claims 119-138 and further, Claims 132 and 133 have been canceled without prejudice or disclaimer for pursuit of this subject matter in subsequent continuation or divisional applications. Further, new Claims 139-145 recite the precise conditions used during hybridization. Accordingly, Applicants submit that the claims are definite and respectfully request that this rejection be withdrawn.

Claim Rejections - 35 U.S.C. §102

Claim 132 and 134 are rejected under 35 U.S.C. §102(b) as being unpatentable over Kobayahi *et al.* (Accession no. D00102- dated 2000). The Examiner asserts that Kobayashi discloses a polynucleotide which is 30% identical to the PRO1097 polynucleotide in the instant application.

In view of cancellation of Claims 132-134, this rejection is obviated and should be withdrawn. Further, Applicants submit that since new Claims 139-142 recite an isolated nucleic acid molecule "at least 20 nucleotides in length" of SEQ ID NO:348 or ATCC accession number 203044 or complements thereof, and further recites **high stringency** hybridization conditions. Thus, the instant Claims 139-142 are not anticipated by Kobayashi et al. Accordingly, this rejection should be withdrawn.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641**, referencing Attorney's Docket No. **39780-2730 P1C62**.

Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: July 30, 2004

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